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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
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08/469,637 08/06/95 GREENE J 325800-381

EXAMINER

18N2/0916

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1100 NEW YORK AVENUE N W
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WASHINGTON DC 20005

ART UNIT	PAPER NUMBER
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1812

17

DATE MAILED: 09/16/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

- ☒ Responsive to communication(s) filed on 5-28-97, PAPER NO. 17
- ☒ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 21-35 is/are pending in the application.
- Of the above, claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 21-35 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☒ Notice of Reference Cited, PTO-892
- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s) 13 & 15
- ☐ Interview Summary, PTO-413
- ☒ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

—SEE OFFICE ACTION ON THE FOLLOWING PAGES—

9/15/97
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1. The ~~preliminary~~ amendment filed 28 May 1997, Paper No. 17, has been entered. Claims 21-35 are pending.

2. Applicant noticed that the specification in the application was missing page 11 and has requested that the original copy of the page 11 be replaced into the specification. The examiner has verified that the original specification was recorded on microfilm and contained page 11. The microfilm copy of page 11 of the specification as originally filed was entered into the application specification. The missing page 11 was lost during the prosecution after the filing of the application.

3. The rejection under 35 U.S.C. 112, first paragraph, because of a lack of a deposit under the terms of the Budapest treaty is withdrawn in light of the submission of the declaration of deposit.

4. The following listing of references in the specification is not a proper information disclosure statement because it is not journal, patent, or publication. References AR7, AS7, AS8, AT8, AR9, AS2, AR10, AS10, AT10, and AR11 were considered but were struck from the form 1449 because they are not proper references for information disclosure statement.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Applicant's arguments filed 28 May 1997, Paper No. 17, have been fully considered but they are not found persuasive.

Claim Rejections - 35 USC § 112

7. Claims 21-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The newly submitted SEQ ID NO:1 and 2 which contain amended sequences is not supported in the specification. Furthermore, the sequence identity of the deposited clone is disclosed in the specification as the original SEQ ID NO:1 and 2.

Applicant submit that a sequence error has occurred and that the newly submitted sequence of SEQ ID NO:1 and 2 are correct. Applicant argue that the deposit No. 75899 inherently comprises the newly submitted sequence. It is suggested that the applicant examine *Ex parte Maizel*, 27 USPQ2d 1662 (BPAI), for support and

submit a declaration establishing the "chain of custody" indicating, for example, such information as, how the error arose, how the error was detected, and how one of ordinary skill in the art could use routine experimentation to recognize and determine the correct sequence from the deposited material.

8. Claims 30 and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the disclosed nucleic acids comprising the sequence encoding SEQ ID NO:2, and allelic variants, does not reasonably provide the full scope of enablement for the whole genus of variants or fragments of polynucleotides encoding SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 30 and 35 encompass fragments and variants of the disclosed sequences because the recitation of "at least 95% identity" and "at least one conservative amino acid substitution". Thus, claim 35 encompasses an unlimited number of amino acid substitutions. The specification fails to teach how to make and use all variants and fragments for the reasons set forth in the last office action.

Applicants argue that computer algorithms are available to the skilled artisan for identifying nucleic acid sequences at least 95% identical to the sequences of the polynucleotides recited in the claims. However, most homology algorithm require adjustment of parameters such as the window of number of nucleic acid examined to gap distances which is not taught in the specification to enable one skilled in the art to determine what is a 95% identity nucleic acid. The state of the art is such that determining the parameters of the algorithm is unpredictable (Bowie et al.(U), page 1308, right column). While one skilled in the art may use algorithm to generate nucleic acid sequence with any percent identity, one must be able to specifically teach what comprises 95% sequence identity and how to use the variants. For the same reasons set forth in the previous office action and argued below, a nucleic acid sequence with at least 70% or 95% identity encode variants which are not enabled.

Applicants argue that the skilled artisan is fully aware of amino acid sequence changes that are either less likely or not likely to significantly affect protein function. Applicants cite Bowie et al.(U) in support of enablement for amino acid substitutions. However, Bowie et al. teach on page 1307, right column, middle paragraph, that no substitutions or only conservative substitutions were allowed. Furthermore, the state

of the art is such that the rules of how a protein folds three-dimensionally is extremely complex, and it seems unlikely that neither the rules nor the predictability of protein structure will be solved in the near future (Bowie et al.(U), page 1307, left column, first paragraph). Thus, it is unpredictable for one skilled in the art to determine whether a variant protein is functional or not based on substituting an amino acid using an algorithm. Any mutagenesis studies requires the actual empirical experimentation to determine whether the protein is functional. Prior to the mutagenesis experiment, it is unpredictable to determine whether variants are functional. Thus, a variant protein with an amino acid substitution generated by an algorithm without actual empirical experimentation cannot determine whether the protein is functional or not. The specification does not provide a reasonably predictable method of determining the amino acid substitution which will result in a functional protein. The specification fails to provide guidance to make an duse variants.

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is

reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Since the fee set forth in 37 CFR 1.17(r) for a first submission subsequent to a final rejection has been previously paid, applicant, under 37 CFR 1.129(a), is entitled to have a second submission entered and considered on the merits if, prior to abandonment, the second submission and the fee set forth in 37 CFR 1.17(r) are filed prior to the filing of an appeal brief under 37 CFR 1.192. Upon the timely filing of a second submission and the appropriate fee for a small entity under 37 CFR 1.17(r), the finality of the previous Office action will be withdrawn. If a notice of appeal and the appeal fee set forth in 37 CFR 1.17(e) were filed prior to or with the payment of the fee set forth in 37 CFR 1.17(r), the payment of the fee set forth in 37 CFR 1.17(r) by applicant will be construed as a request to dismiss the appeal and to continue prosecution under 37 CFR 1.129(a). In view of 35 U.S.C. 132, no amendment considered as a result of payment of the fee set forth in 37 CFR 1.17(r) may introduce new matter into the disclosure of the application.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Pak whose telephone number is (703) 305-7038. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308-2957. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the

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examiner should be directed to (703) 308-0294.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**stephen.walsh@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MDP

Michael D. Pak
1812
10 September 1997

Stephen Walsh
STEPHEN WALSH
SUPERVISORY PATENT EXAMINER
GROUP 1800